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10/682,130	10/07/2003	Dennis M. Klinman	4239-66902-01	1348

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EXAMINER	
ARCHIE, NINA	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/682,130	**Applicant(s)** KLINMAN ET AL.
	Examiner Nina A. Archie	**Art Unit** 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 22 August 2007.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7,10-30 and 33-48 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) 1-7,10-30 and 33-41 is/are rejected.
7)☒ Claim(s) 48 is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 10, 2007 has been entered.

Amendment Entry

2. The amendment filed August, 22, 2007 has been entered. Claims 1, 19-20, and 23 have been amended. Claims 8-9, 31-32, and 42 have been cancelled.

Withdrawal of Rejection

3. The rejection of claims 1-7, 10-30, and 33-41 under 35 U.S.C. 112, first paragraph (written description rejection) has been withdrawn in view of applicant's amendments and arguments.

Response to Arguments

4. Applicant's arguments with respect to claims 1-3, 15, 17-19 and 40 have been considered but are moot in view of the rejections in the previous office action.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7, 10-30, and 33-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating inflammatory lung disease, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide SEQ ID NO. 1 to a subject having or at risk of developing inflammatory lung disease in vivo, does not reasonably provide enablement for an *in vitro* method of treating inflammatory lung disease, comprising administering a therapeutically effective amount of suppressive oligodeoxynucleotide comprising SEQ ID NOs. 2-25. Furthermore, the specification does not reasonably enable an *in vivo* method of inhibiting inflammatory lung disease in a subject, animal or human, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotides to a subject having or at risk of developing inflammatory lung disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Applicant's Arguments

Claims 1-7, 10-30, and 33-41 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification. Applicants thank the Examiner for stating that that the specification is enabling for a method of treating inflammatory lung disease by administering a therapeutically effective amount of an oligodeoxynucleotide (ODN) with the nucleic acid sequence set forth as SEQ ID NO: 1. Each of the points raised in the Examiner's Response to the [previous] Arguments by the Applicants (see page 5-8 of the Office action) are addressed below:

A) The Office action accepts that the claims are limited to specified ODNs, and that the claims are limited to methods of treatment. However, the Office action asserts that the claimed methods are only enabled for the use of ODNs of the lengths shown in Table 1; as a specific oligodexoynucleotide of 10 nucleotides in length is not shown in

Table 1, one of skill in the art allegedly could not make an ODN of 10 nucleotides in length that is effective. Applicants respectfully disagree with this assertion.
However, solely to advance prosecution, the claims are limited to the use of ODNs of at least 12 nucleotides in length and at most 30 nucleotides in length. Applicants note that an exemplary ODN sequence of use that is 12 nucleotides in length is specifically listed in Table 1 (see SEQ ID NO: 6); the remaining ODN sequences (SEQ ID NOs: 1-5 and SEQ ID NOs: 7-25) shown in Table 1 are less than 30 nucleotides in length. Thus, the amendments to the claims render the rejection moot.

B) The Office action acknowledges that the methods for the treatment of inflammatory lung disease are enabled by the specification. However, the Office action asserts that the Applicants have not demonstrated prevention of lung disease. Thus the Office action asserts that the inhibition of lung disease using the claimed ODNs is not enabled by the specification. Applicants respectfully disagree with this assertion. Applicants note that by "treating" inflammatory lung disease, the symptoms of the disease would be inhibited. In addition, by "preventing" inflammatory lung disease, the symptoms of the disease would be inhibited. Solely to advance prosecution, the claims have been amended to recite that claimed methods are for "treating" inflammatory lung disease, thereby rendering the rejection moot.

C) The Office action confirms that the synthesis of ODNs is well known in the art, and that the administration of these ODNs is also known in the art. The Office action also confirms that there are art-recognized models of inflammatory lung disease.

D) The Office action confirms that the level of skill of one of ordinary skill in the art, such as a molecular biologist or pulmonologist is high.

E) The Office action confirms that there are art recognized models, formulations, and that routes of administration are routine. However, the Office action again asserts that only methods of treatment that utilize a more limited set of ODNs are enabled by the specification. These assertions were addressed under A and B above.

F) The Office action confirms that specific characteristics of ODNs of use have been provided in the specification, that pharmaceutical compositions and methods of administering these ODNs are provided, and that methods for confirming the effectiveness of an ODN of use are provided. However, the Office action asserts that no methods for preventing inflammatory lung disease are provided, and that no specific nucleotide sequences in the lower range (10 nucleotides) were provided. As noted in points A and B, the amendment of the claims renders these rejections moot.

G) The Office action acknowledges the presentation of a number of working examples, such as on page 21 and in SEQ ID NOs: 1-25, and confirms that working examples of the treatment of an inflammatory disease are presented in the Examples section. However, the Office action states that there is no working example "for treating inflammatory lung disease in vitro" or for "preventing inflammatory lung disease." As the claims are amended herein to be limited to methods of treating inflammatory lung disease in a subject, Applicants believe that these rejections are moot (see also A and B above).

H) The Office action acknowledges that there is ample guidance provided on the synthesis of ODNs and for formulations for the delivery of ODs. However, the Office action states that there is no working example "for treating inflammatory lung disease in vitro" and states that there is only guidance for "treating inflammatory lung disease in vivo." As the claims are amended herein to be limited to methods of treating inflammatory lung disease in a subject, Applicants believe that the claims are directed to the subject matter considered enabled by the Examiner (see also A, B and G, above). The claims as amended are directed to subject matter that was confirmed by the Examiner to be enabled by the specification. As such, reconsideration and withdrawal of the rejection is respectfully requested.

Examiner's Response to augments

5. A) It is noted that the Office action accepts that the claims are limited to specified ODNs, and that the claims are limited to methods of treatment. However, the Office action asserts that the claimed methods are only enabled for the use of ODNs of the lengths shown in Table 1.

B) The Examiner accepts that the claims are directed to methods of treatment that utilize nucleic acid sequences. As discussed previously, the state of the art indicates that the state of the art for treating and preventing inflammatory lung disease are using current treatments such as anti-inflammatory medications. Although inflammatory lung disease can be treated there is no treatment for recurrence or prevention of the full development of the disease. The standard therapy for treating inflammatory lung disease is corticosteroids. However they also have limitations in their treatment and cannot inhibit inflammatory lung disease (see Broide et al 1998 Immunostimulatory DNA Sequences Inhibit IL-5, Eosinophilic Inflammation, and Airway Hyperresponsiveness in Mice The Journal of Immunology p. 7054 and Bernard GR 2005 Acute respiratory distress syndrome: a historical perspective. *American Journal Respiratory Critical Care Med.* 2005 Oct 1;172(7):798-806). Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without under experimentation.

C) The examiner accepts that the synthesis of ODNs is well known in the art, as is the administration of ODNs to a subject of interest and that there are art-recognized models for testing therapies for the treatment of inflammatory lung disease.

(D) The examiner accepts that the level of ordinary skill in the art is of a molecular biologist and/or pulmonologist is high.

(E) The examiner accepts that there are art recognized models for inflammatory lung disease (such as the one described in the examples section) that can be used to confirm the effect of an ODN of interest and the administration of agents to a subject for the treatment of inflammatory lung disease is described (see the specification, page 24, line 9 to page 30, line 10). The examiner accepts the pharmaceutical formulations and methods of administration are routine to one of skill in the art. However the examiner disagrees that the level of predictability in the art and the production of ODNs with specified characteristics is routine. The specification teaches a method of treating inflammatory lung disease with suppressive oligodeoxynucleotides in a subject.

(F) The examiner accepts the amount of direction provided in the specification: The specification discloses the physical characteristics of ODNs of use, namely that they (1) are at least 12 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 15-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). General classes of ODNs that have these characteristics are provided (see the specification on page 21, lines 1-10), and at least 25 examples of suppressive ODNs are provided (see the specification on page 21, lines 11-21, and SEQ ID NOs: 1-25). In addition, pharmaceutical compositions and methods of administration of ODNs are described in the specification (see page 24, line 9 to page 30, line 10). Methods for confirming the effectiveness of an ODN, such as by monitoring lung function are disclosed (see the specification at page 30, line 11 to page 31, line 15).

G) The examiner accepts working examples of the ODNs of use described in the specification (see, for example, page 21, lines 15-21 and SEQ ID NOs: 1-25). The examiner accepts the effectiveness of these ODNs in inhibiting an immune response in vitro as disclosed in Example 2. The examiner accepts the use of ODN (SEQ ID NO: 1) in an animal model of inflammation is described in the specification as disclosed in Example 3. However there is no working example for treating inflammatory lung disease in vivo. Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without under experimentation.

(H) The examiner accepts that there is substantial guidance provided on the synthesis of ODNs and formulation of ODNs for delivery to a subject (see, for example, page 19, line 26 to page 24, line 7). The examiner accepts that the synthesis of ODNs is automated and routine. There is only guidance to the method of treating inflammatory lung disease in vivo.

New Grounds of Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention. This is a written description rejection.

6. Claims 1-7, 10-30, 33-41, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claim is drawn to a method of treating inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing inflammatory lung disease, wherein the suppressive oligodeoxynucleotide is at least about 12 nucleotides and at most 30 in length, forms a G-tetrad, has a CD value of greater than 2.9, and comprises at least two guanosines, thereby treating the inflammatory lung disease. The recitation of "at least about least 12 and at most 30 nucleotides in length", “forms a G-tetrad”, and “at least two guanosines” does not convey a common structure. Further the claim recites open claim language and the exact structure of the vast genus of suppressive oligodeoxynucleotide cannot be envisioned. The oligonucleotides recited in the pending claimed genus would not clearly apprise one skilled in the art that the inventors had possession of the claimed genus and all species encompassed thereby as of the filing date. The structure of these oligonucleotides has not been specifically defined. The claims do not set forth the specific structure of the claimed oligonucleotides and it is not clear if the claims or specification give the structure and a function of the oligonucleotide, as required by written description guidelines.

The claims are drawn to a vast genus of oligonucleotides. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a “laundry list” disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not “reasonably lead” those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) (“If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.”) (emphasis in original). In Ex parte Ohshiro, 14 USPQ2d 1750 (Bd. Pat. App. & Inter. 1989), the Board affirmed the rejection under 35 U.S.C. 112, first paragraph, of claims to an internal combustion engine which recited “at least one of said piston and said cylinder (head) having a recessed channel.” The Board held that the application, which disclosed a cylinder head with a recessed channel and a piston without a recessed channel did not specifically disclose the “species” of a channeled piston.

In conclusion, the specification provides no guidance or description on the structure of the suppressive oligodeoxynucleotide that has the function that the application claims in the methods. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is needed. Since the disclosure fails to describe the structural characteristics that determine if any suppressive oligodeoxynucleotide can be used in treating or inhibiting inflammatory lung disease in a subject (human or otherwise) effectively, this is a written description rejection.

Claim 1-7, 10-30, 33-41, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim recites the phrase “at least 12-30 nucleotides”. Although Applicant filed an explanation in the Applicants Arguments/Remarks on 8/22/2007. A single example of a sequence having 12 nucleotides for example (SEQ ID NO: 6) does not provide support for the genus of any nucleotide sequence having at least 12 nucleotides, forming a G-Tetrad and CD value of ab 2.9 and comprises at least two guanosines, thereby treating the inflammatory lung disease. Therefore, it is apparent, that Applicants were not in possession of the claimed genus at the time of filing. This is a new matter rejection.

Conclusion

Status of the Claims

7. Claims 43-47 are allowed.
Claims 1-7, 10-30, and 33-41 are rejected.
Claim 48 is objected to as being dependent upon a rejected base claim.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina Archie
Examiner
Art Unit 1645

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